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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/649,480	08/27/2003	Thomas J. Stegmann	CVGENG.008CP1	5376

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EXAMINER	
LI, BAO Q	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 11/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/649,480	STEGMANN ET AL.	
	Examiner	Art Unit	
	Bao Qun Li	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 August 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,12,16-34 and 36* is/are pending in the application.

4a) Of the above claim(s) *16,18 and 19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,12,17, 20-34 and 36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *07/14/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

This is a response to the amendment filed 08/25/05. Claims 1 and 26 have been amended. Claims 2-11, 13-25 and 35 have been canceled. Claims 1, 12, 16, 17-34 and 36 are pending before the examiner. Claims 1, 12, 17-34 and 36 in the scope of SEQ ID NO: 6 and 7 are considered by the examiner.

Please note any ground of rejection(s) that has not been repeated is removed. Text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Election/Restrictions

1. This application contains claim 1 in the scope of SEQ ID Nos: 1, 3 and 4 drawn to an invention nonelected with traverse filed on April 18, 2005. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Priority

2. The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

3. The disclosure of the prior-filed application, Application No. 09/358/780 and 60/093,962, fails to provide adequate support or enablement of claim 1 in the manner provided by the first paragraph of 35 U.S.C. 112.

4. In the instant case, the sequences in the amended claim 1 are only supported by the disclosure of application 60/225,406, which is filed on August 15, 2000. Therefore, the priority of the amended claim 1 and its dependent claims are considered to be August 15, 2000.

Declaration

5. The **Declaration** by Dr. Stegmann under 37 CFR 1.131 filed on August 25, 2005, has been acknowledged. However, the declaration is insufficient to overcome the rejection, because in view of the new amended of claim 1,the primary reference by Schumacher et al. (Circulation, Feb, 1998, Vol. 97, pp. 645-650) is a statutory bar under 35 U.S.C. 102(b) and thus cannot be overcome by an affidavit or declaration under 37 CFR 1.131.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1, 12, 17, 20-34 and 36 are still rejected under 35 U.S.C. 103(a) under the same ground as stated in the previous Office Action, as being unpatentable over Schumacher et al. (Circulation, Feb, 1998, Vol. 97, pp. 645-650) for claims 1, 3-11, 13-15, 20-22, 33 and 36, Jaye et al. (US Patent No. 5,571,790A) and Fasol et al. (J. Thorac Cardiovasc. Surg. 1994, Vol. 107, pp. 1432-1439).

8. In response to the previous Office action, applicant amended claim 1 and also filed Declaration under 37 CFR 1.131 to overcome the primary reference by Schumacher et al. published on Circulation, on Feb. 1998.

9. The **Declaration** by Dr. Stegmann under 37 CFR 1.131 filed on August 25, 2005, has been acknowledged. However, the declaration is insufficient to overcome the rejection. Because in view of the amended claim 1, said primary reference by Schumacher et al. (Circulation, Feb, 1998, Vol. 97, pp. 645-650) is a statutory bar under 35 U.S.C. 102(b) and thus cannot be overcome by an affidavit or declaration under 37 CFR 1.131.

10. In the instant case, the sequences in the amended claim 1 are only supported by the disclosure of application 60/225,406, which is filed on August 15, 2000. Therefore, the priority of the amended claim 1 and its dependent claims are considered to be August 15, 2000. Consequently, the primary reference by Schumacher et al. (Circulation, Feb, 1998, Vol. 97, pp. 645-650) is published more than one year than the prior date of the rejected claims 1, 12, 16-34 and 36. Therefore, said reference by Schumacher et al. is a 102(b) reference that cannot overcome by an affidavit or declaration under 37 CFR 1.131. Hence the rejection is maintained.

New ground rejections:

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 1, 12 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pu et al. (Circulation 1993, Vol. 88, No. 1, pp. 208-215), Linemeyer et al (US patent NO. 5,401832A) and Kordyum et al. (US Patent No. 6,773,899B2).

13. Claims 1, 12 and 17 are directed to a method for recascularizing an ischemic region comprising preparing a composition comprising a recombinant fibroblast growth factor –1 (FGF-1), and injecting it into the ischemic region, wherein said FGF-1 is either the polypeptide comprising the amino acid sequence of SEQ ID NO: 7 or the polypeptide comprising the amino acid sequence of SEQ ID NO: 7 from position 2 to position 141 or a polypeptide encoded by a gene comprising the sequence of SEQ ID NO: 6.

14. Pu et al. teach a method of revascularization in the ischemic rabbit limb comprising to apply endothelial cell growth factor (ECGF, which is a synonym of FGF) to the ischemic limb area. The treatment significantly accelerates the revascularization in

the ischemic limbs (See abstract and Figs. 1-5). Pu et al. do not teach precise sequence structure of the FGF-1.

15. Linemyer et al. disclose the exactly same human FGF-1 polypeptide sequence, wherein the amino acid residues of said polypeptide has 100% identical to the amino acid residues of 2-141 of the claimed human FGF-1 of claim 7 and amino acid sequences as claimed drafted (In fact, HECGF is an synonym of FGF). In addition, Linemyer et al. teaches that the said Recombinant Human FGF-1 is used for promoting cell growth, healing and recascularization of grafted blood vessel (See Table 1 and abstract).

16. Kordyum et al. disclose the exactly nucleic acid sequence (SEQ ID NO: 6 and and its deduced amino acid sequence that is 100% identical to the claimed nucleic acid sequence of SEQ ID NO: 6 and amino acid sequence of claimed SEQ IFD NO: 7, Moreover, Kordyum et al. disclose that said nucleic acid sequence encodes the polypeptide named as ECGF (Previous name of FGF-1) has similar function as native isolated human FGF-1 that has a potential in the treatment of the damage or regeneration of blood vessel or endothelial cell-line structure (See SEQ ID NO: 6 and column 14, example 6).

17. Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention was filled to be motivated by the recited references and to treat ischemic tissue injury in view of the disclosures by Pu et al. to treat ischemic region with the polypeptide disclosed by Linemyer et al. or Kordyum et al. Because the all of the references teach that human FGF is able to recascularizing the blood vessel. Hence the claimed invention as a whole is prima facie obvious absence unexpected results.

18. Claims 1, 12, 17 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Banai et al. (Cir. Res. 1991, Vol. 69, No. 1, pp. 76-85), Linemeyer et al (US patent NO. 5,401832A) and Kordyum et al. (US Patent No. 6,773,899B2).

19. Claims 1, 17 and 36 are directed to a method for recascularizing an ischemic region of art comprising preparing a composition comprising a recombinant fibroblast growth factor –1 (FGF-1), and injecting it into the ischemic region, wherein said FGF-1 is either the polypeptide comprising the amino acid sequence of SEQ ID NO: 7 from

position 2 to position 141 or is the polypeptide encoded by a gene comprising the sequence of SEQ ID NO: 6.

20. Banai et al. disclose a method for improving blood circulation in an experimental ischemic myocardium comprising administration of acidic fibroblast growth factor (FGF-a) onto the myocardium of the dogs experimentally suffered from ischemic myocardial infarctions. They have demonstrated that FGF-a stimulates a striking smooth muscle cell hyperplasia in all arteries and small arteries exclusively in area of subendocardial infarctions, and administration of FGF-a into the myocardium of the dogs compromises the reduced coronary flows in the ischemic area because the FGF-stimulates vascularization of all smooth muscle cells in the ischemic areas (See abstract and Figs. 1-8). Banai et al. do not teach precise sequence structure of the claimed FGF-1.

21. Linemyer et al. disclose the exactly same human FGF-1 polypeptide sequence, wherein the amino acid residues of said polypeptide has 100% identical to the amino acid residues of 2-141 of the claimed human FGF-1 of claim 7 and amino acid sequences as claimed drafted (In fact, HECGF is an synonym of FGF). In addition, Linemyer et al. teaches that the said recombiant Human FGF-1 is used for promoting cell growth, healing and recascularization of grafted blood vessel (See Table 1 and abstract).

22. Kordyum et al. disclose the exactly nucleic acid sequence (SEQ ID NO: 6 and its deduced amino acid sequence that is 100% identical to the claimed nucleic acid sequence of SEQ ID NO: 6 and amino acid sequence of claimed SEQ IFD NO: 7, Moreover, Kordyum et al. disclose that said nucleic acid sequence encodes the polypeptide named as ECGF (Previous name of FGF-1) has similar function as native isolated human FGF-1 that has a potential in the treatment of the damage or regeneration of blood vessel or endothelial cell-line structure (See SEQ ID NO: 6 and column 14, example 6).

23. Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention was filled to be motivated by the recited references and to treat ischemic tissue injury in view of the disclosures by Banai et al. to treat ischemic region with the polypeptide disclosed by Linemyer et al. or Kordyum et al. Because the all of the references teach that human FGF is able to recascularizing the blood vessel. Hence the claimed invention as a whole is prima facie obvious absence unexpected results.

24. Claims 1, 12, 17 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Htun et al. (J. Mol. Cell. Cardiol. April 1998, Vol. 30, pp. 867-877), Linemeyer et al (US patent NO. 5,401832A) and Kordyum et al. (US Patent No. 6,773,899B2).

25. Claims 1, 17 and 36 are directed to a method for recascularizing an ischemic region in the art comprising preparing a composition comprising a recombinant fibroblast growth factor –1 (FGF-1), and administering it into the ischemic region, wherein said FGF-1 is either the polypeptide comprising the amino acid sequence of SEQ ID NO: 7 from position 2 to position 141 or is the polypeptide encoded by a gene comprising the sequence of SEQ ID NO: 6.

26. Htun et al. teach a method of treating or preventing pig myocardium suffered ischemic damage. The method comprises administering directly the human recombinant FGF-1 or FGF-2 into the myocardium via a direct intramyocardium infusion. Htun et al. do not teach precise sequence structure of the claimed FGF-1.

27. Linemyer et al. disclose the exactly same human FGF-1 polypeptide sequence, wherein the amino acid residues of said polypeptide has 100% identical to the amino acid residues of 2-141 of the claimed human FGF-1 of claim 7 and amino acid sequences as claimed drafted (In fact, HECGF is an synonym of FGF). In addition, Linemyer et al. teaches that the said Lrecombiant Human FGF-1 is used for promoting cell growth, healing and recascularization of grafted blood vessel (See Table 1 and abstract).

28. Kordyum et al. disclose the exactly nucleic acid sequence (SEQ ID NO: 6 and its deduced amino acid sequence that is 100% identical to the claimed nucleic acid sequence of SEQ ID NO: 6 and amino acid sequence of claimed SEQ IFD NO: 7, Moreover, Kordyum et al. disclose that said nucleic acid sequence encodes the polypeptide named as ECGF (Previous name of FGF-1) has similar function as native isolated human FGF-1 that has a potential in the treatment of the damage or regeneration of blood vessel or endothelial cell-line structure (See SEQ ID NO: 6 and column 14, example 6).

29. Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention was filled to be motivated by the recited references and to treat ischemic tissue injury in view of the disclosures by Htun et al. to treat ischemic region

with the polypeptide disclosed by Linemyer et al. or Kordyum et al. Because the all of the references teach that human FGF is able to recascularizing the blood vessel. Hence the claimed invention as a whole is prima facie obvious absence unexpected results.

30. Claims 1, 12, 17, 23-27, 34 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fasol et al. (J. Thorac Cardiovasc. Surg. 1994, Vol. 107, pp. 1432-1439).), Linemeyer et al (US patent NO. 5,401832A) and Kordyum et al. (US Patent No. 6,773,899B2).

31. Claims 12, 17, 23-27, 34 and 36 are directed to a method for recascularizing an ischemic region comprising preparing a composition comprising a recombinant fibroblast growth factor –1 (FGF-1), fibrin glue and anticoagulant, and injecting it into the ischemic region, wherein said FGF-1 comprises the amino acid sequence of SEQ ID NO: 7 from position 2 to position 141 or is encoded by a gene comprising the sequence of SEQ ID NO: 6.

32. Fasol. Et al. teach a method of using heparin-binding growth factor (HBGF) or α and β endothelial cell growth factors (α and β ECGF) (synonym of FGF) for inducing site directed angiogenesis in animal model comprises administering a composition comprising a recombinant HBGF or α or β ECGF in combinations with fibrin and heparin into the hear wall during the surgical experiments. They teach a similar surgical procedure for the open hear surgery comprising making a thoracotomy incision, accessing to the myocardium of the left ventricle via a small incision into the pericardium, and placing the composition to the left ventricular myocardium. They found that the administration of the composition comprising FGF induce a significant blood vessel growth and addition of fibrin glue in the composition meets the conditions of being an easily available substance for applying the angiogenesis growth factor to the target organ, which has the conditional advantage of clinical applicability (See pages 2-3, 4-5, Fig. 4, pages 7-10). Fasol et al. do not teach precise sequence structure of the claimed FGF-1.

33. Linemyer et al. disclose the exactly same human FGF-1 polypeptide sequence, wherein the amino acid residues of said polypeptide has 100% identical to the amino acid

residues of 2-141 of the claimed human FGF-1 of claim 7 and amino acid sequences as claimed drafted (In fact, HECGF is an synonym of FGF). In addition, Linemyer et al. teaches that the said Lrecombiant Human FGF-1 is used for promoting cell growth, healing and recascularization of grafted blood vessel (See Table 1 and abstract).

34. Kordyum et al. disclose the exactly nucleic acid sequence (SEQ ID NO: 6 and its deduced amino acid sequence that is 100% identical to the claimed nucleic acid sequence of SEQ ID NO: 6 and amino acid sequence of claimed SEQ IFD NO: 7, Moreover, Kordyum et al. disclose that said nucleic acid sequence encodes the polypeptide named as ECGF (Previous name of FGF-1) has similar function as native isolated human FGF-1 that has a potential in the treatment of the damage or regeneration of blood vessel or endothelial cell-line structure (See SEQ ID NO: 6 and column 14, example 6).

35. Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention was filled to be motivated by the recited references and to treat ischemic tissue injury in view of the disclosures by Fasol et al. to treat ischemic region with the polypeptide disclosed by Linemyer et al. or Kordyum et al. Because the all of the references teach that human FGF is able to recascularizing the blood vessel.

36. Regarding to the dosage of anticoagulation agent or fibrin glue, it is routine agent used in the clinic for a person skilled in the art. Hence the claimed invention as a whole is prima facie obvious absence unexpected results.

Conclusion

No claims are allowed.

37. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 571-272-0904. The examiner can normally be reached on 7:00 am to 3:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Bao Qun Li
11/10/2005

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